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ANALYSIS OF KIDNEY STONES IN THE SUBMARINE FORCE

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Naval Medical Research and Development Command
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SUMMARY PAGE

PROBLEM:

To retrospectively examine nephrolithiasis waiver and disqualification packages in both the Atlantic and Pacific Submarine Fleets.

FINDINGS:

Medical Officers noted metabolic and environmental conditions predisposing to stone formation in 53% of the individuals. Hypercalciuria (29%) hyperuricosuria (22%) and hypocitraturia (9%) were the most frequently documented disturbances. Analysis of individual laboratory values revealed a greater percentage of abnormalities than noted by Medical Officers. Hypercalciuria (36%), hyperuricosuria (33%), hyperphosphaturia (32%), hypocitraturia (19%), elevated urinary sodium (12%), and low urine volume (57%) were the most common laboratory abnormalities. Individuals with no documented predisposition to stone formation, recurrent stone-formers, submariners with retained stones, and personnel from the Pacific Fleet were less likely to be waived of physical stnadards (P values < 0.05).

APPLICATION:

Results indicate that the incidence of metabolic abnormalities in the submarine force is greater than expected and the majority of stone patients have a treatable condition. Personnel with waivers for nephrolithiasis will need to be followed prospectively over several years to determine additional information (such as recurrence rates with appropriate treatment) and the operational impact of maintaining these individuals' submarine qualifications.

ADMINISTRATIVE INFORMATION

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Abstract

This report presents the results of a retrospective review of nephrolithiasis waiver and disqualification packages submitted to Atlantic and Pacific Force Medical Officers over the past three years. General characteristics of stone-formers in the Submarine Force are described. Medical Officers noted metabolic and environmental conditions predisposing to stone formation in 53% of the individuals. Hypercalciuria (29%), hyperuricosuria (22%), and hypocitraturia (9%) were the most frequently documented disturbances. Analysis of individual laboratory values revealed a greater percentage of abnormalities than noted by Medical Officers. Hypercalciuria (36%), hyperuricosuria (33%), hyperphosphaturia (32%), hypocitraturia (29%), elevated urinary sodium (12%), and low urine volume (57%) were the most common laboratory abnormalities. Individuals with no documented predisposition to stone formation, recurrent stone-formers, submariners with retained stones, and personnel from the Pacific Fleet were less likely to be waived of physical stnadards (P values < 0.05). Results indicate that the incidence of metabolic abnormalities in the submarine force is greater than expected and the majority of stone patients have a treatable abnormality. Personnel with waivers for nephrolithiasis will need to be prospectively followed over several years to determine additional information (such as recurrence rates with appropriate treatment) and the operational impact of maintaining these indiividuals' submarine qualifications.

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ANALYSIS OF KIDNEY STONES IN THE SUBMARINE FORCE

Background

Until recently, 40 to 60 submariners were medically disqualified annually from submarine duty because of kidney stones (nephrolithiasis), resulting in the loss of experienced individuals to the submarine force. This policy has recently been liberalized in conjunction with a prospective clinical study being conducted by the Naval Submarine Medical Research Laboratory (NSMRL) and endorsed by the Chief, Bureau of Medicine and Surgery (1).

In 1989, Postma and Quinn (2) rev iewed renal stone waiver and disqualification packages submitted to Commander Submarine Force Atlantic Fleet (COMSUBLANT) during a 16 month period. They found that the average amount of experience lost to the submarine force per disqualification was 8.75 years and concluded that the policy regarding the disposition of submariners with kidney stones should be liberalized in favor of medical waiver. This recommendation was subsequently endorsed by the COMSUBLANT Force Medical Officer in 1989.

The revised guidance (3), issued in 1990, recommended that waivers should <u>not</u> be recommended for those submariners with retained stones, recurrent stones, stones failing to pass spontaneously, and a solitary calcareous stone with no demonstrable treatable abnormality on standardized workup (Figure 1). Waivers could be obtained for first time stone formers with a correctable metabolic abnormality. Correctable abnormalities would include environmental conditions such as dehydration and high consumption of protein, sodium, and calcium, and metabolic abnormalities resulting in hypercalciuria or hypocitraturia.

This extensive evaluation for first-time stone formers was adapted from several reviews of the pathogenesis and treatment of nephrolithiasis (4,5). Although many clinicians agree that all single stone formers should be evaluated, there is disagreement on the scope of the investigation. Wilson (6) suggested in a recent review that the initial evaluation include a medical history, serum testing for calcium, phosphorus, uric acid, and creatinine, an intravenous pyelogram (IVP) with tomographic cuts, a first morning urine pH and gram stain, and urine culture if indicated. He did not recommend performing 24-hour urine studies as part of the evaluation. Ryall and Marshall (7) essentially agree with this approach. Preminger (8,9) believes that an extensive evaluation is indicated for single stone formers at "high risk" for recurrence, a group including

Figure 1. Evaluation of Stone Formers in the Submarine Force

Family History of Nephrolithiasis

Dietary History:
- Fluid intake, animal protein, drug and vitamin use

Laboratory Data:
- Serum Chemistry Panel
- Urinalysis
- Urine Culture (only during acute episode)
- 24 Hour Urine calcium x 2, uric acid x 2, sodium x 2, creatinine x2, oxalate x 1, citrate x 1 and volume x 2 on unrestricted diet
- Qualitative urinary cystine
- Morning urinary pH for 5 consecutive days
- Chemical Analysis of Calculus if available
- Calcium fast and load study after 7 day on calcium and sodium-restricted diet

Radiographic Studies:
- Intravenous pyelography

white middle age males with a family history of stone disease. His suggested evaluation includes three 24-hour urine collections over a two week period including tests of urine calcium, uric acid, citrate, oxalate, volume, pH, and sodium. A review by Uribarri (10) recommends a single 24-hour urine study measuring calcium, uric acid, volume, pH, and citrate for first time stone formers. Given the potential operational impact of an episode of nephrolithiasis while underway, medical officers concede that a rigorous evaluation of these individuals is indicated.

There has been considerable progress in the diagnosis and treatment of specific metabolic abnormalities leading to nephrolithiasis. Civilian literature has shown a high incidence of metabolic abnormalities in single stone formers, ranging from 50 to 80 percent. Strauss et al. (11) examined 182 patients with a single calcium renal stone and found that 51.1% had idiopathic hypercalciuria (elevated urinary calcium levels not attributed to known factors such as increased dietary intake of calcium or increased renal excretion of calcium) or hyperuricosuria and 19.8% had other systemic disorders predisposing to stones. Only 29% had no evidence of a metabolic abnormality in this

study. Pak (12) obtained similar results when examining 34 patients with a single episode of stone formation. Absorptive hypercalciuria was found in 55.9% (23.5% type I and 32.4% type II), renal hypercalciuria in 11.8%, primary hyperparathyroidism in 2.9%, hyperuricosuric calcium oxalate in 8.8% and no metabolic abnormality in only 20.6%. These studies suggest that the majority of stone formers have an environmental (e.g. dehydration, elevated dietary consumption of calcium) or physiological disturbance causing a predisposition to nephrolithiasis.

Preliminary unpublished data from the submarine force indicated that 70-80% of submariners with renal stones had normal metabolic evaluations. It is not known whether this difference reflects a different patient population or a less rigorous evaluation.

The purpose of this study is to review the characteristics of stone disease in the submarine force over the past 3 years. Incidence of various metabolic and environmental abnormalities will be emphasized.

Methods

One-hundred fifty-two nephrolithiasis waiver and disqualification packages submitted to the Atlantic and Pacific Force Medical Officers over approximately 3 years were reviewed. In most cases, waiver packages are prepared by either Group or Squadron medical personnel. The evaluation is coordinated by the patients medical officer and may include specialty evaluation by a urologist or other specialists. Based on the results of the evaluation, the medical officer will then recommend a waiver or disqualification to the individual's Commanding Officer. The Commanding Officer will then make a recommendation through the chain of command which includes the Force Medical Officer (COMSUBLANT or COMSUBPAC) and Chief of the Bureau of Medicine and Surgery (BUMED). Waivers are granted only by Naval Military Personnel Command (NMPC). A submariner that is recommended for waiver of physical standards by the local medical officer may be disqualified at any point in the chain of command. Only rarely is a recommendation for disqualification reversed by a higher authority.

Cases were excluded if minimal diagnostic criteria for nephrolithiasis (typical renal colic and microscopic hematuria) were not met or information in the record cast doubt on the diagnosis. Demographic information (Pacific or Atlantic fleet), medical history (medications, concurrent and past medical illnesses, allergies), family history of nephrolithiasis, dietary history, and race were extracted from the records if available.

Particular attention was given to the metabolic evaluation. Results of serum studies (for electrolytes, blood urea nitrogen, creatinine, calcium, uric acid, and phosphorus), 24-hour urine samples (for total volume, calcium, uric acid, citrate, phosphorus, sodium, oxalate, and cystine), and calcium fast and load studies were recorded. Abnormal results were based on the performing laboratory's reference values. The clinical interpretation of the metabolic evaluation by the medical officer was noted. Chemical composition of recovered stones was recorded. Treatment protocols initiated as well as success or failure of treatments for metabolic abnormalities were examined.

Data was extracted using standardized forms and entered into a database using Systat 5.0 statistical software. Categorical variables were compared using the chi-square or Fisher exact test. These tests were selected to distinguish significant group differences between individuals either waived or disqualified.

Results

General Characteristics

One-hundred thirty-six packages met established case criteria for nephrolithiasis. Characteristics of stone-formers in the submarine fleet are displayed in Table 1. The mean age of the subjects at the time of stone-formation was 29.7 years. One-hundred twenty-four (91%) were enlisted personnel. Eighty-three (61%) packages were submitted from the Atlantic Fleet. Family history of nephrolithiasis in a first-degree relative was present in 23% when elicited. Medical evacuation was necessary in 6 (4.4%) of the cases, all occurring in first time stone-formers. A metabolic abnormality was noted to be present by the medical officer in 63 (53% of cases where this information was available) of the cases. Extra corporeal shock wave lithotripsy or surgical/cystoscopic removal of a stone was required in 16 (11.8%) of the cases. For the group of recurrent stone-formers (13%), the average time between recurrence was 3.1 years.

Table 1. General Characteristics of Stone-Formers in the Submarine Force

Characteristic	Number (%)
Status	
Enlisted	124 (91)
Officer	12 (9)
Race	
Caucasian	123 (96)
Negroid	5 (3.9)
Fleet	
Atlantic	83 (61)
Pacific	53 (39)
Family History of nephrolithiasis	27 (20)
Number resulting in MEDEVAC	6 (4.4)
Stone Analysis Available	41 (30)
Retained stone on radiograph	9 (8.3)
First-time stone former	118 (87)
Documented metabolic abnormality	63 (53)
Cases requiring ESWL	9 (6.6)
Requiring surgical or cystoscopic removal	7 (5.2)
Documented anatomic abnormality	7 (5.2)
Recurrent stone formers	18 (13)
Average time between recurrence, *yrs*	3.1

Metabolic and Environmental Risk Factors

Risk factors for stone-formation were reported by the Medical Officer in 53% (n=119) of the cases (Table 2). Hypercalciuria was present in 29% and hyperuricosuria in 22% of the cases. Results are also reported for the remaining metabolic (hypocitraturia, hyperoxaluria) and environmental (low urine volume, hyperphosphaturia, and elevated urinary sodium) risk factors occurring as both a sole disturbance and in combination with other abnormalities.

Table 2. Classification of Nephrolithiasis Risk Factors By Medical Officers

	Total # (%)	Sole Occurrence(%)	Combined Occurrence(%)
Hypercalciuria	34 (29)	16	13
Hyperuricosuria	26 (22)	10	12
Hypocitraturia	11 (9)	3	6
Hyperphosphaturia	6 (5)	<2	3
Hyperoxaluria	1 (<1)	<1	-
Decreased volume	5 (4)	2	2
Elevated Urine Na	3 (3)	<1	2
No Abnormality	56 (47)	-	-

Laboratory Analysis

Results of metabolic evaluation independent of the individual medical officer's interpretation of the laboratory results are presented in Table 3. Based on individual laboratory reference values, the most frequently encountered abnormalities found were hypercalciuria (36%), hyperuricosuria (33%), and hyperphosphaturia (32%). When urine volume was standardized to a normal value of > 1500 ml./day, more than one-half (57%) of these measurements were abnormally low. Hypocitraturia (19%) and elevated urinary sodium (12%) were less frequent. One case of hyperoxaluria was diagnosed by a physician based on a borderline urinary oxalate despite a value within the normal range. The one abnormal oxalate value was disregarded based on a previously normal value. Serum calcium and uric acid were elevated in 3% of patients tested.

Table 3. Laboratory Results on Initial Evaluation

	# Tests	# Abnormal (%)
Urinary calcium (mg./day)	105	38 (36)
Urinary uric Acid (mg./day)	99	33 (33)
Urinary citrate (mg./day)	63	12 (19)
Urinary phosphorus (mg./day)	44	14 (32)
Urine volume < 1500 ml./day	106	60 (57)
Urinary sodium (meq/day)	60	7 (12)
Urinary oxalate (mg./day)	69	1 (1)
Urinary cystine (mg./day)	37	5*
Serum uric acid (mg./dl.)	90	3 (3)
Serum calcium (mg./dl.)	102	3 (3)

* Includes 1 positive qualitative test

Waiver -vs- Disqualification

Various characteristics of submariners waived or disqualified for nephrolithiasis were compared independently (Table 4). Officers were more likely to be waived of physical standards than enlisted personnel. Significantly more personnel were disqualified in the Pacific Fleet. Although not statistically significant because of the small number, it was noted that no black submariners were waived.

Those individuals with treatable metabolic or environmental abnormalities were more likely to be waived than those with no identified disturbance. No subjects with retained stones were waived and recurrent stone-formers were less likely to be waived. Treatment success or failure was based on documented correction of metabolic or environmental abnormalities. It was noted that appropriate medical treatment of these abnormalities was usually successful.

Table 4. Characteristics of Waiver and Disqualification

Characteristic	Disqualified	Waived	P Value
Status, *n* (%)			
Enlisted	78 (57)	46 (34)	0.046
Officer	4 (3)	8 (6)	
Race, *n* (%)			
White	70 (55)	53 (41)	
Black	5 (4)	-	
Fleet, *n* (%)			
Atlantic	41 (30)	42 (31)	
Pacific	41 (30)	12 (9)	0.001
Metabolic Abnormality, *n*(%)			
Absent	40 (34)	16 (13)	0.001
Present	25 (21)	38 (32)	
Retained Stone, *n* (%)			
No retained stone	51 (47)	49 (45)	
Retained stone	9 (8)	-	
Recurrence, *n* (%)			
First stone	67 (49)	51 (38)	
Recurrent stone	15 (11)	3 (2)	0.032
Results of Treatment, *n* (%)			
Not successful	2 (6)	3 (9)	
Successful treatment	8 (24)	21 (62)	

Discussion

Our study documents a greater incidence of metabolic and environmental abnormalities in submariners with nephrolithiasis than was previously estimated by submarine medical officers. In fact, the majority of patients were found to have a potentially treatable abnormality. The incidence of abnormalities, however, is still considerably lower than that reported in the civilian literature where extremely thorough laboratory evaluations were conducted (11,12). One explanation for this difference is that the great majority of submarine evaluations were incomplete when compared to the standards used in civilian studies. Most evaluations also fell far short of the Force Medical requirements (3), although some were submitted before these guidelines were disseminated to all Submarine Medical Officers. If Medical Officers were able to complete the entire evaluation, the

incidence of abnormalities would likely be greater.

The multiple 24-hour urine collections required were the most frequently omitted tests in these evaluations. The calcium fast-and-load studies -- currently required in all cases even if hypercalciuria is absent -- were not administered in a standardized fashion. "Tums" and "Yogurt", for example, were used for calcium loading in some cases, rather than the standardized 1 gram dose of calcium mixed in a synthetic meal recommended in the original reference (15). The five day urine pH measurements were done only sporadically and performed with urine dipsticks, rather than the pH electrode recommended by other investigators (16). The time to complete the entire evaluation was often greater than one month, leading to frustration for both the practitioner and the submariner awaiting a decision on his duty status. A simplified evaluation would be welcomed by the Medical Officers and the submariners undergoing evaluation.

There were also difficulties in the interpretation of laboratory results. These problems were seen most commonly with 24-hour urine studies. As our population is spread throughout the United States, Europe, and Asia, a large number of military and civilian laboratories with different collection standards and reference values were used. The "normal" values for 24-hour urine studies were not standardized and showed great variation. Urine volume values as low as 550 ml. were not flagged or interpreted as abnormally low. A number of abnormal laboratory results were apparently not felt to be clinically significant by Medical Officers. The use of a single or small group of reference laboratories specialized in urine testing may improve the accuracy of these tests and lessen difficulties with the interpretation of results.

These results suggest that an extensive, but streamlined, investigation for metabolic and environmental abnormalities predisposing to nephrolithiasis should be conducted. Testing for hypercalciuria, hyperuricosuria, hyperphosphaturia, hypocitraturia, increased urinary sodium and decreased urine volume is certainly warranted, comprising most abnormalities. Multiple urine pH measurements (not accurate unless a pH electrode can be used) can be replaced by 24-hour urine pH and citrate measurements, which will identify those individuals with a urine acidification defect. Qualitative spot urine testing for cystinuria, followed by quantitative measurement of positive test results, would identify rare cases of this condition. The calcium fast and load tests should be replaced by a Sodium Cellulose Phosphate Screening Test (9), which does not require calcium loading. This test should

only be performed in those cases where hypercalciuria persists despite dietary restrictions.

Generally, multiple 24-hour urine tests are not necessary during the initial evaluation. Pak (16) suggests a full analysis be performed on a single 24-hour urine specimen. If any risk factors are identified, a sample can be repeated following appropriate dietary restriction. All 24-hour urine collections should measure creatinine to ensure the collection was complete.

Although treatment regimens for these conditions were not standardized, the results suggest that the majority of cases with abnormalities can be successfully treated. This data is consistent with results from the civilian literature. Pak (12) reports metabolic control (remission) in > 95% of cases in patients treated with "selective" medical therapy for mild to moderate stone disease. In an older study, Frank et al. (13) found that solely increasing urinary output from approximately 800 ml. to 1200 ml. per day decreased the incidence of urinary calculus by 86%. Our population is extremely motivated and would likely adhere to treatment protocols. As stone-formers return to the submarine force it will be possible to study more closely the efficacy of treatment for individual abnormalities.

It was not feasible to accurately estimate recurrence rates of stone-formers with this data. The number of recurrent formers was small and follow-up information was not available on every subject. A prospective study currently underway at this laboratory will track recurrence rates for stone-formers retained on submarine duty.

The limitations of this study are those of retrospective reviews. Non-standardization of laboratory results and missing data elements were most problematic. Additional useful information concerning recurrence rates, metabolic abnormalities, and effectiveness of treatment would be gained by prospectively following submariners in this unique environment.

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